

## IL-1 ETA DNA AND POLYPEPTIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

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sub c1 > This application is a continuation in part of United States applications Serial Numbers 60/135,758, 60/162,331, and PCT/US00/14455, filed May 25, 1999, October 29, 1999, and May 25, 2000, respectively. The entire disclosures of these applications are relied upon and incorporated by reference herein.

BACKGROUND OF THE INVENTIONField of the Invention

10 The invention is directed to novel, purified and isolated IL-1 eta polypeptides and fragments thereof, the polynucleotides encoding such polypeptides, processes for production of recombinant forms of such polypeptides, antibodies generated against these polypeptides, fragmented peptides derived from these polypeptides, and uses thereof.

Description of Related Art

20 Interleukin-1 (IL-1) is a member of a large group of cytokines whose primary function is to mediate immune and inflammatory responses. There are seven known IL-1 family members which include IL-1 alpha (IL-1 $\alpha$ ), IL-1 beta (IL-1 $\beta$ ), IL-1 receptor antagonist (IL-1ra), IL-1 delta (IL-1 $\delta$ ), IL-1 epsilon (IL-1 $\epsilon$ ), IL-1 zeta (IL-1 $\xi$ ) and IL-18 (previously known as IGIF and sometimes IL-1 gamma). IL-1 that is secreted by macrophages is actually a mixture of mostly IL-1 $\beta$  and some IL-1 $\alpha$  (Abbas et al., 1994). IL-1 $\alpha$  and IL-1 $\beta$ , which are first produced as 33 kD precursors that lack a signal sequence, are further processed by proteolytic cleavage to produce secreted active forms, each about 17 kD. Additionally, the 33 kD precursor of IL-1 $\alpha$  is also active. Both forms of IL-1 are the products of two different genes located on chromosome 2. Although the two forms are less than 30 percent homologous to each other, they both bind to the same receptors and have similar activities.

30 IL-1ra, a biologically inactive form of IL-1, is structurally homologous to IL-1 and binds to the same receptors. Additionally, IL-1ra is produced with a signal sequence which allows for efficient secretion into the extracellular region where it competitively competes with IL-1 (Abbas et al., 1994).

The IL-1 family of ligands binds to a family of two IL-1 receptors, which are members of the Ig superfamily. IL-1 receptors include the 80 kDa type I receptor (IL-1RI) and a 68 kDa type II receptor (IL-1RII). IL-1 ligands can also bind to a soluble proteolytic fragment of IL-1RII (sIL-1RII) (Colotta et al., 35 1993).

The major source of IL-1 is the activated macrophage or mononuclear phagocyte. Other cells that produce IL-1 include epithelial and endothelial cells (Abbas et al., 1994). IL-1 secretion from macrophages occurs after the macrophage encounters and ingests gram-negative bacteria. Such bacteria contain